WHAT IS CLAIMED IS:

1. A peptide of the formula R^1-Asp-Lys-Gly-X-Y-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-X'-Y'-R^2 SEQ ID NO:1, wherein said Thr is not glycosylated,

wherein R^1 is a moiety having a net positive charge other than L-Val;

wherein R^2 is selected from the group consisting of a free hydroxyl, an amide, an imide, a sugar, and a sequence of one or up to about 15 additional amino acids, optionally substituted with a free hydroxyl, an amide, an imide or a sugar, said additional amino acids being independently selected from L-configuration or D-configuration and said additional amino acids capable of cyclizing the peptide by bridging between the N- and C- termini thereof;

wherein X and Y form a dipeptide selected from the group consisting of Ser-Tyr and a dipeptide formed of naturally occurring amino acids or unnatural amino acids, said dipeptide resistant to cleavage; and

wherein X' and Y' form a dipeptide selected from the group consisting of Asn-Arg, and a dipeptide formed of naturally occurring amino acids or unnatural amino acids, said dipeptide resistant to cleavage.

2. The peptide according to claim 1, wherein R^1 is selected from the group consisting of

(a) a straight chain, branched, cyclic or heterocyclic alkyl group,

(b) a straight chain, branched, cyclic or heterocyclic alkanoyl group,

(c) a positively charged reporter group; and

(d) between 1 to 15 additional amino acids independently selected from L-configuration or D-configuration; said additional amino acids optionally substituted by one or more of (a), (b) or (c), and said additional amino acids capable of cyclizing the peptide by bridging between the N- and C- termini thereof.

3. The peptide according to claim 2, wherein said R^1 group (d) are amino acids which have been cyclized by the insertion into the structure of the amino acid of modifying sugars or imide.

4. The peptide according to claim 2, wherein said R^1 group (a) is 1-aminocyclo-hexane carboxylic acid.

5. The peptide according to claim 2, wherein said R^1 group (d) is selected from the additional amino acid residues D-Val-, Arg-Val-, Lys-Val-, Lys-Val-Asp-Lys-Val-, and -Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-Val-.

6. The peptide according to claim 1, wherein said R^1 group is selected from Acetyl-Arg-Val-; Acetyl-Lys-Val-; and Acetyl-Lys-Val-Asp-Lys-Val-.

7. The peptide according to claim 2, wherein said R^1 group (c) is biotin.

8. The peptide according to claim 2 wherein said R^1 group provides a detectable signal, optionally upon interaction with other compounds.

9. The peptide according to claim 8 wherein said R^1 group (c) is 5(6) carboxyfluorescein.

10. The peptide according to claim 2 wherein R^1 group (c) is radioactive.

11. The peptide according to claim 2 wherein R^1 group (d) is a spacer interposed between the N- terminus and C- terminus of said peptide, permitting cyclization of said peptide.

12. The peptide according to claim 11, wherein R^1 group (d) is -Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-Val- SEQ ID NO: 3, said Val linked to the N-terminal Asp of said formula and the N-terminal amino acid of R^1 linked by a covalent bond to the C-terminal amino acid of R^2.

13. The peptide according to claim 1, wherein R^2 is selected from the group consisting of D-Asn, L-Asn, Asp, and Asn-R^3, wherein R^3 is a sugar.

14. The peptide according to claim 1, wherein said R^2 is an amino acid can cyclize the peptide by attaching to the amino terminal amino acid.

15. The peptide according to claim 13 wherein R^3 is selected from the group consisting of 2-acetamido-2-deoxyglucose and triacetyl 2-acetamido-2-deoxyglucose.

16. The peptide according to claim 1, wherein R^2 is a β-acetyl-2,3-diamino propionic acid group.

17. The peptide according to claim 1, wherein at least one amino acid is altered to its corresponding D amino acid.

18. The peptide according to claim 1, which is non-glycosylated.

19. The peptide according to claim 1, which is a cyclic peptide in which R^1 and/or R^2 form an amino acid spacer of greater than 3 amino acid residues.

20. The peptide according to claim 19, wherein said spacer duplicates at least a portion of the peptide sequence of claim 1.

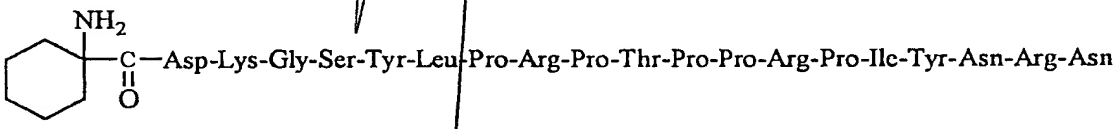
21. The peptide according to claim 1, which is:
Val-Asp-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO:30.

22. The peptide according to claim 1, which is:
Acetyl-Lys-Val-Asp-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO: 7.

23. The peptide according to claim 1, which is :
Acetyl-Arg-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO:8.

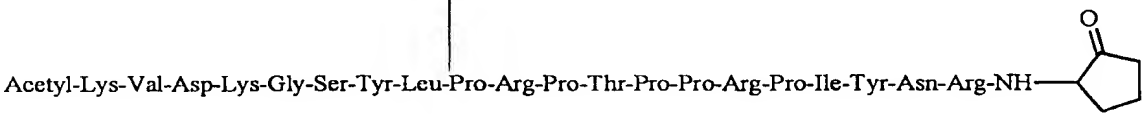
24. The peptide according to claim 1, which is:
Acetyl-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO: 9.

25. The peptide according to claim 1, which is:



SEQ ID NO:10.

26. The peptide according to claim 1, which is:



SEQ ID NO: 12.

27. The peptide according to claim 1, which is:
Acetyl-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-NH-CH-$CONH_2$ SEQ ID NO: 13.
|
CH_2-NH-$COCH_3$

28. The peptide according to claim 1, which is:
Acetyl-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO: 14.
|
2-acetamido-2-deoxyglucose

29. The peptide according to claim 1, which is:
Acetyl-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO:15.
|
triacetyl-2-acetamido-2-deoxyglucose

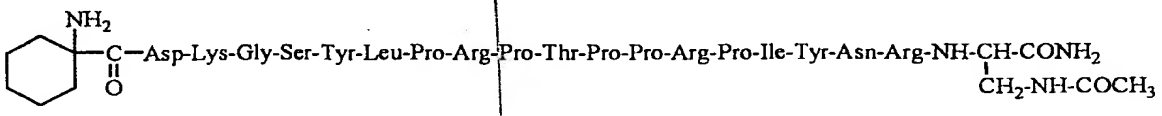
30. The peptide according to claim 1, which is
D-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-D-Asn SEQ ID NO: 16.

31. The peptide according to claim 1, which is:
Biotin-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO:19.

32. The peptide according to claim 1, which is:
5(6)-carboxyfluorescein-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asn SEQ ID NO: 20.

33. The peptide according to claim 1, which is:
Acetyl-Lys-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-Asp SEQ ID NO: 21.

34. The peptide according to claim 1, which is:



SEQ ID NO: 22.

35. The peptide according to claim 1, which is:

Acetyl-Arg-Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-NH-CH-CONH$_2$ SEQ ID NO: 23.

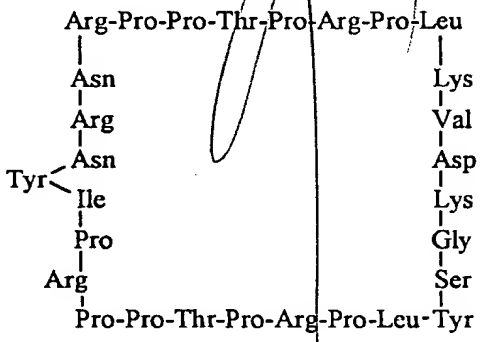
CH_2-NH-$COCH_3$

36. The peptide according to claim 1, which is:

Val-Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg-NH-CH-CONH$_2$ SEQ ID NO:25.

CH_2-NH-$COCH_3$

37. The peptide according to claim 18, which is:



SEQ ID NO:18.

38. The peptide according to any of claims 1-37 which has metabolic stability in mammalian serum.

39. The peptide according to claim 1 wherein at least one conventional amide bond between two amino acids in said sequence is replaced with a non-cleavable bond.

40. The peptide according to claim 39, wherein said non-cleavable bond is a thio-amide bond or a reduced amide bond.

41. A composition comprising multiple peptides of the formula R^1-Asp-Lys-Gly-X-Y-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-X'-Y'-R^2 SEQ ID NO: 1,

wherein R^1 is a moiety having a net positive charge;

wherein R^2 is selected from the group consisting of:

(a) a free hydroxyl, an amide, an imide, or a sugar;

(b) a sequence of one or up to about 5 additional naturally occurring or unnatural amino acids, optionally substituted with a free hydroxyl, an amide, an imide or a sugar,

(c) a sequence of (b) wherein said additional amino acids cyclize the peptide by bridging between the N- and C- termini thereof; and

(d) a sequence of (b), wherein said additional amino acids link at least two said peptides;

wherein X and Y form a dipeptide selected from the group consisting of Ser-Tyr and a dipeptide formed of naturally occurring amino acids or unnatural amino acids, said dipeptide resistant to cleavage,

wherein X' and Y' form a dipeptide selected from the group consisting of Asn-Arg, and a dipeptide formed of naturally occurring amino acids or unnatural amino acids, said dipeptide resistant to cleavage.

42. The composition according to claim 41, comprising at least two peptides, wherein the second peptide is attached to any amino acid of the first peptide.

43. The composition according to claim 42, wherein additional peptides are attached to any amino acid of the other peptides in the composition.

44. The composition according to claim 41, comprising at least two said peptides, wherein at least one or more of said peptides is attached to a carrier.

45. The composition according to claim 41, comprising at least two peptides of claim 1, wherein the second or additional peptides is attached to a branched construct of the other peptides in the composition.

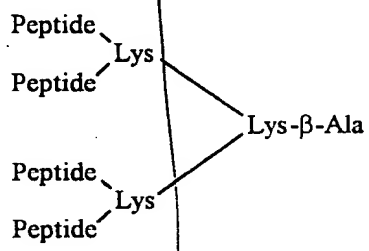
46. The composition according to claim 41, comprising at least two peptides of claim 1, wherein each additional peptide is covalently linked to R^2 of another peptide in the composition.

47. The composition according to claim 41, which is a multiple antigenic peptide.

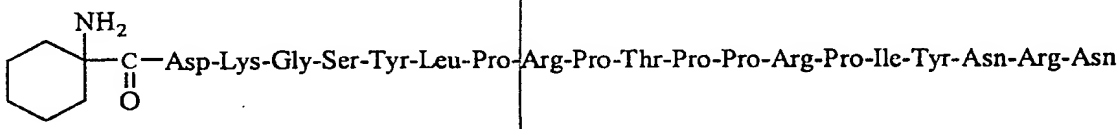
48. The composition according to claim 47, wherein said multiple antigenic peptide comprises a β-alanine substituent on a poly-lysine core.

49. The composition according to claim 47, comprising at least four peptides.

50. The composition according to claim 49, comprising the structure

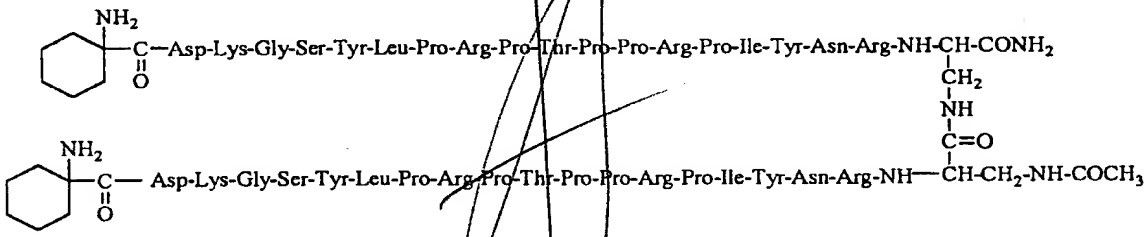


wherein each said peptide is:



SEQ ID NO: 10.

51. The composition according to claim 41, comprising the multi-peptide SEQ ID NO: 4 construct



52. The composition according to claim 41 wherein said peptide is produced synthetically.

53. The composition according to claim 41 wherein said peptide is produced recombinantly.

54. The composition according to claim 41 wherein one or more of said peptides is a synthetic peptide fused to a second moiety, wherein said moiety enhances the bioavailability of said peptide.

55. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a peptide of claim 1 or multi-peptide composition of claim 41 in operative association with a regulatory sequence directing the expression thereof in a host cell.

56. A host cell transfected or transformed with the molecule of claim 55.

57. A pharmaceutical composition comprising one or more of the peptides of claim 1 or the compositions of claim 41, in a pharmaceutically acceptable carrier.

58. A method of treating a mammalian infection comprising administering to a mammal having said infection an effective amount of a composition of claim 57.

59. The method according to claim 58, wherein said infection is a bacterial infection.

60. The method according to claim 58 wherein said infection is caused by a Gram negative bacterium.

61. The method according to claim 58 wherein said infection is caused by a Gram positive bacterium.

62. The method according to claim 58, wherein said infection is a fungal infection.

63. The method according to claim 58 wherein said composition is administered by a route selected from intravenous, oral, intradermal, transdermal, intraperitoneal, intramuscular, subcutaneous, by inhalation and mucosal.

64. A method of treating a mammalian infection comprising administering to a mammal having said infection a low dose of a pharmaceutical composition comprising deglycosylated pyrrhocoricin.

65. The method according to claim 64, wherein said infection is a bacterial infection.

66. The method according to claim 64, wherein said infection is a fungal infection.

67. The method according to claim 64, wherein said low dose is less than 10 mg/kg patient body weight.

68. A method for designing pharmaceutical compounds comprising:

employing a peptide of claim 1 or a composition of claim 41 in a computer modeling program to design a compound which mimics the structure and biological effect of said peptide or composition.

69. The method for identifying pharmaceutical compounds comprising:

performing a competitive assay with a microorganism susceptible to a peptide of claim 1 or a composition of claim 41; a peptide of claim 1 or a composition of claim 41, and at least one test compound; and

identifying said test compound which competitively displaces the binding of said peptide or said composition to a receptor on said microorganism.

70. The method according to claim 69, wherein said microorganism is a bacterium.

71. The method according to claim 69, wherein said microorganism is a fungus.

72. A compound produced or identified by the method of claim 68 or 69.

73. The peptide according to claim 1, which is fused to a second protein.

74. A composition according to claim 41, wherein R^2 of one said peptide is a β-acetyl-2,3- diamino propionic acid group and wherein an additional said peptide is linked to the same R^2 at the carboxyl terminus.

75. A peptide of the formula R^1-Asp-Lys-Gly-X-Y-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-X'-Y'-R^2 SEQ ID NO:1, wherein said Thr is not glycosylated,

wherein R^1 is a moiety having a net positive charge;

wherein R^2 is selected from the group consisting of a free hydroxyl, an amide, an imide, a sugar, and a sequence of one or up to about 15 additional amino acids, optionally substituted with a free hydroxyl, an amide, an imide or a sugar, said additional amino acids being independently selected from L-configuration or D-configuration and said additional amino acids capable of cyclizing the peptide by bridging between the N- and C- termini thereof;

wherein X and Y form a dipeptide selected from the group consisting of Ser-Tyr and a dipeptide formed of naturally occurring amino acids or unnatural amino acids, said dipeptide resistant to cleavage; and

wherein X' and Y' form a dipeptide selected from the group consisting of Asn-Arg, and a dipeptide formed of naturally occurring amino acids or unnatural amino acids, said dipeptide resistant to cleavage.